prolonged unconsciousness, and trauma. In this study, none of the patients had cardiac symptoms, and we feel that the elevated cTnI levels may have been due to causes other than myocardial ischaemia.

False positive cTnI often causes unnecessary anxiety and over diagnosis of myocardial infarction. By misrepresenting the implications of cTnI elevation, this study gives rise to a diagnostic dilemma that could lead to a wastage of health resources, as well as inappropriate investigations, which may cause unnecessary morbidity. An integration of cardiac biomarkers (CK, CKMB, cTnI), ECG and comprehensive echocardiographic systolic and diastolic function assessments (wall motion score index),[4] and, if indicated, nuclear medicine scans,[5] will better identify false positive cTnI elevations and will avoid inappropriate admissions to coronary care units. Clinical context must be carefully considered before investigating this group of patients for coronary artery disease.

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Reply to Correspondence from V.S. Jeganathan and S. Walker Re: Peri-operative Myocardial Injury in Patients Undergoing Surgery for Critical Limb Ischemia. S.D. Hobbs, M. Yapanis, P.J. Burns, A.B. Wilmink, A.W. Bradbury, D.J. Adam. Eur J Vasc Endovasc Surg 2005; 29: 301–304

We thank Jeganathan and Walker for their interest in our study, however, we are concerned that they have failed to fully understand the pathophysiological and prognostic significance of elevated levels of cardiac troponin (cTn) I. Their assertion that the results of our study must be viewed with caution due to possible 'false positive cTnI elevations' is largely unfounded. Several medical conditions are associated with elevations in cTnI level and the underlying mechanism is invariably myocardial cell death. To illustrate this point, we will take the examples provided by Jeganathan and Walker individually:

- Acute coronary syndrome with evidence of raised cTnI is diagnostic of myocardial injury.
- In the case of myocarditis and pericarditis, it is active inflammation in or around the heart that leads to myocardial necrosis and subsequent elevation of cardiac troponin levels.[1]
- In moderate to severe pulmonary embolism, elevated cTnI levels occur in approximately one in seven patients and are believed to be a consequence of myocardial damage secondary to an acute rise of right ventricular afterload and systemic hypoxemia.[2]
- In subjects with end stage renal failure (ESRF) requiring dialysis elevated cardiac troponin levels are thought to be due to a combination of uraemic myocarditis and cardiac micro-infarctions as well as impaired renal excretion.[3] Elevations in cTnI, however, are uncommon as demonstrated by a large series of 733 subjects with ESRF where only 0.4% were shown to have cTnI levels at a level diagnostic of myocardial injury.[4] None of the subjects in our study had ESRF.
- The absence of cTnI in foetal and healthy or diseased adult skeletal muscle[5] implies that elevated levels of cTnI do not occur as a result of rhabdomyolysis. Furthermore, cTnI has been demonstrated to be a valuable biomarker for the detection of sub-clinical myocardial damage in

patients with rhabdomyolysis secondary to trauma.[6]

- Whilst we agree that factors such as heterophile antibodies (HA) can cause interference in immunoassays (such as that used to assay cTnI) and thus produce true false positives, the incidence of interfering HAs is low.[7] Furthermore, the majority of studies assessing the prognostic significance of cTnI make no effort to screen and correct for HAs.

Our study demonstrated that up to one third of patients undergoing bypass surgery for critical lower limb ischaemia (CLI) sustained peri-operative myocardial injury as manifest by an elevated cTnI. Regardless of the mechanism of injury, it is clear that myocardial cell damage occurs in a significant proportion of these patients and there is abundant evidence to demonstrate that acute elevations in cTnI are associated with adverse short and long-term prognosis in patients undergoing major vascular surgery.[8,9] Jeganathan and Walker are keen to stress the importance of clinical context when investigating patients with CLI for coronary artery disease. This group has such a high incidence of coronary artery disease that further treatment of those patients experiencing a cTnI rise seems entirely appropriate.

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Effect of Macrolides on Peripheral Arterial Disease Depends on Patient Selection and Adequate Treatment

Vainas *et al.* investigated a possible effect of a 3-day azithromycin course on peripheral arterial disease (PAD) during 2 years. Peripheral arterial complications were observed in 23% of azithromycin-treated and 20% of placebo-treated patients. Vainas *et al.* concluded that a short-term course of azithromycin does not influence PAD.[1] In contrast, our group showed that administration of roxithromycin for 28 days prevents progression of PAD in *Chlamydia pneumoniae* seropositive men. Limitation of walking distance to 200 m or less was observed in 20% of roxithromycin-treated and 65% of placebo-treated patients. Five invasive revascularizations were carried out in 20% of roxithromycin-treated patients compared to 29 interventions in 45% of placebo-treated patients during 2.7 years.[2]

The striking difference between the two studies regarding the effect of macrolides on PAD needs explanation. Patients were selected differently for the two studies. Vainas *et al.* selected patients who either had an IgA titer >16 (mean 28) EIUs or were *C. pneumoniae* seronegative. In contrast, an IgG titer $\geq 1/128$ was inclusion criterion of our study, median *C. pneumoniae* antibody titers were 1/256 (IgG) and 1/64 (IgA). The percentage of patients undergoing severe impairment of PAD clearly differed between the placebo group of Vainas' study (20%) and our study (65%). Duration of antibiotic treatment was different in the two studies. Azithromycin administered for 3 days—though characterized by a serum and tissue half life time of several days—is expected to have a less accentuated